The opinion in support of the decision being entered today is not binding precedent of the Board.

Paper 116 39

By: Trial Section Merits Panel
Board of Patent Appeals and Interferences
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
Tel: 703-308-9797
Fax: 703-305-0942

Filed: July 16, 2003

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

---

QUIG WANG, MITCHELL H. FINER
and XIAO-CHI JIA

Junior Party,
Application 08/333,680

v.

JEAN-LUC IMLER, MAJID MEHTALI
and ANDREA PAVIRANI

Senior Party,
Application 09/218,143



---

Patent Interference No. 104,821 (CAS)

---

Before: TORCZON, SPIEGEL and MILLS, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

**MEMORANDUM OPINION and FINAL JUDGMENT**
**(Decision on remaining preliminary motions)**

## I. Introduction

This is a decision on the remaining preliminary motions filed by parties Wang

and Imler in Interference 104,821 following oral arguments on March 25, 2003. Steven B. Kelber, Esq., Linda Judge, Esq. and Sue Jensen, M.D., appeared for party Wang. Todd R. Walters, Esq., Susan M. Dadio, Esq. and Christopher L. North, Ph.D., appeared for party Imler.

Interference 104,821 involves recombinant replication-defective[1] adenoviral vectors[2] wherein an "essential" function of the E2A early gene region,[3] i.e., one necessary for viral viability or normal growth is rendered nonfunctional by a lethal mutation[4] in the adenoviral genome, e.g., by deleting all or a part of the E2A gene.

Wang has filed three preliminary motions. Imler has filed ten responsive preliminary motions. Wang preliminary motion 1, seeking a judgment of no interference-in-fact, has been denied (Paper 28).

---

[1] A replication-defective [or deficient] viral vector is a viral vector that is unable to replicate due to deficiencies in gene functions essential for replication (i.e., generation of viral progeny) to occur. Such viral vectors are able to replicate in complementing cell lines that provide the missing gene functions in *trans* or with the aid of a helper virus. [Paper 39, "IMLER SUBMISSION OF GLOSSARY AND CHART," hereinafter "Glossary," p. 8.]

[2] An adenoviral vector is an adenovirus that can carry a heterologous nucleic acid sequence (i.e., a transgene) into a suitable host cell. A transgene is a gene that is not normally present in a cell or viral vector, also called a heterologous or foreign gene. A gene is a physical and functional unit of heredity, which carries information from one generation to the next. In molecular terms, a gene is the entire DNA sequence necessary for the synthesis of a functional polypeptide or RNA molecule. In addition to coding regions, most genes also contain non-coding intervening sequences (introns) and transcription-control regions. [Glossary, pp. 1, 4 and 9.]

[3] The early region is an area of the adenoviral genome that contains adenovirus genes expressed before the onset of viral DNA replication. Early region transcripts may continue to be synthesized after the onset of viral DNA replication. The early region is divided into the E1A, E1B, E2A, E2B, E3 and E4 regions. [Glossary, p. 3.]

[4] A mutation is a deletion, insertion and/or substitution of one or more nucleotides in a nucleic acid sequence. A lethal mutation is any mutation that may bring about death or an inability to grow in an organism, virus or viral vector before it matures. [Glossary, p. 6.]

Wang preliminary motion 2 attacks the benefit for the purpose of priority accorded Imler of U.S. application 08/379,452, PCT application PCT/FR94/00624 and French application FR93/06482 as to Count 1 of the interference. Wang preliminary motion 3 seeks judgment that all of Imler's involved claims are unpatentable for failure to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. We grant Wang preliminary motions 2 and 3.

Imler's preliminary motions may be divided into two sets, i.e., motions 1 through 5 and motions 6 through 10.

Imler preliminary motion 2 seeks to add proposed Imler claims 66 and 67. Imler preliminary motion 1 seeks to add proposed Count 2, directed to recombinant adenoviruses/vectors having deletions and/or mutations in both the E1 and E4 regions, and to designate Wang claims 37-38, 46-47 and 56 and proposed Imler claims 66 and 67 as corresponding to proposed Count 2. Imler preliminary motions 3 through 5 seek benefit for the purpose of priority of U.S. application 08/379,452, PCT application PCT/FR94/00624 and French application FR93/06482, respectively, as to proposed Count 2. We grant Imler preliminary motion 2 and dismiss Imler preliminary motions 1 and 3 through 5, subject to the APJ taking further appropriate action.

Imler preliminary motions 6 through 10 are contingent upon the grant of Wang preliminary motion 2 or 3. Imler preliminary motion 7 seeks to add proposed Imler claims 68 and 69. Imler preliminary motion 6 seeks to substitute proposed Count 3, directed to recombinant adenoviruses/vectors with deletions in E1 and E2A (with Wang claims 46 and 56 corresponding) or in E1 and all or part of E2 (with proposed Imler

claims 68 and 69 corresponding), for present Count 1. Imler preliminary motions 8 through 10 seek benefit for the purpose of priority of U.S. application 08/379,452, PCT application PCT/FR94/00624 and French application FR93/06482, respectively, as to proposed Count 3. We deny Imler preliminary motions 6 and 7 and dismiss Imler preliminary motions 8 through 10.

## II. Findings of fact

The following findings of fact are supported by a preponderance of the evidence.

1. The junior party is Quig Wang, Mitchell H. Finer and Xiao-Chi Jia (**Wang**).

2. Wang is involved in the interference on the basis of U.S. application 08/333,680 (Wang '680), filed November 3, 1994.

3. Wang's real party-in-interest is Cell Genesys, Inc.

4. The senior party is Jean-Luc Imler, Majid Mehtali and Andrea Pavirani (**Imler**).

5. Imler is involved in the interference on the basis of U.S. application 09/218,143 (Imler '143), filed December 22, 1998.

6. Imler '143 has been accorded benefit for the purpose of priority of

   a. U.S. application 08/379,452 (Imler '452), filed January 26, 1995,

   b. PCT application PCT/FR94/00624 (Imler PCT), filed May 27, 1994 and

   c. French application FR 93 06482 (Imler FR '482), filed May 28, 1993.

7. Imler's real party-in-interest is Transgene S.A.

8. The subject matter of the interference is defined by one count.

9. Count 1 (Paper 1, p. 5) reads:

> The recombinant adenoviral vector of claim 46 of the '680 Wang application, wherein the two gene regions are E1 and E2A

or

The recombinant adenovirus of claim 56 of the '143 Imler application

or

The recombinant adenoviral vector of claim 62 of the '143 Imler application.

10. Wang '680 claim 46 reads:

> A recombinant adenoviral vector, wherein said vector comprises at least a lethal deletion or mutation in two gene regions selected from the group consisting of the E1, E2A and E4 early gene regions; and additionally comprises a transgene so that when rescued the resulting recombinant adenovirus requires for replication at most complementation of genes of the E1, E2A and E4 adenoviral early gene regions.

11. Imler '143 claim 56 reads:

> A recombinant adenovirus comprising an adenovirus genome having a foreign gene and a promoter for expressing said foreign gene, wherein the function of an E2A gene is completely deleted by removing a part or all of said E2A gene.

12. Imler '143 claim 62 reads:

> A recombinant adenoviral vector comprising an adenovirus genome having a foreign gene and a promoter for expressing said foreign gene, wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene.

13. The claims of the parties which have been designated as corresponding to Count 1 are:

| | |
|---|---|
| Wang | 46 and 56 |
| Imler | 56-57, 59 and 61-65 |

14. The claims of the parties which have been designated as <u>not</u> corresponding to Count 1, and therefore are not involved in the interference, are:

| | |
|---|---|
| Wang | 37-45, 47-48, 52, 54 and 57 |
| Imler | none |

15. Imler '143 (Ex 2002) is a continuation of Imler '452 (2008) which is the national

stage entry of Imler PCT (Exs 1003 (French language) & 1004 (certified English language translation)). Except for their respective claims of priority, the specifications of Imler '143, Imler '452 and Imler PCT, including figures, are identical.

16. Imler PCT (Exs 1003 & 1004) claims priority to Imler FR '482 (Exs 1005 (French language) & 1006 (certified English language translation)).

17. All pending Imler claims, i.e., claims 56-57, 59 and 61-65, recite a replication-defective recombinant adenovirus/adenoviral vector "wherein the function of an E2A gene is completely deleted by removing a part or all of said E2A gene."

Other findings of fact follow below.

## III. Wang preliminary motion 3

Wang moves pursuant to 37 CFR § 1.633(a) for judgment that Imler claims 56-57, 59 and 61-65 are unpatentable under 35 U.S.C. § 112, first paragraph (written description), contending that Imler '143 "teaches the deletion of 'all or part of E2', or deletion of E2, but never, E2A" (Paper 34, p. 11). Imler opposes (Paper 64); Wang replies (Paper 102).

To satisfy the written description requirement of the first paragraph of § 112, the specification must convey to one of skill in the art that the inventors had possession of the claimed subject matter at the time of filing. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). "One shows that one is 'in possession' of the invention by describing the invention, with all its claimed limitations." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Put another way, one skilled in the art, reading the original disclosure,

must reasonably discern the limitation at issue in the claims. Waldemar Link GmbH & Co. v. Osteonics Corp., 32 F.3d 556, 558, 31 USPQ2d 1855, 1857 (Fed. Cir. 1994).

The written description requirement is distinct from the enablement requirement. In re DiLeone, 436 F.2d 1404, 168 USPQ 592 (CCPA 1971). Stated somewhat differently, the specification may contain a disclosure that is sufficient to enable one skilled in the art to make and use the invention, and yet fail to comply with the written description of the invention requirement. In re Barker, 559 F.2d 588, 591, 194 USPQ 470, 472 (CCPA 1977), cert. denied, 434 U.S. 1064, 197 USPQ 271 (1978).

In our opinion, Imler '143 neither explicitly discloses nor reasonably conveys to one skilled in the art that Imler was in possession of a replication-defective recombinant adenovirus/adenoviral vector "wherein the function of an E2A gene is completely deleted by removing a part or all of said E2A gene."

**A. There is no original "ipsissimis verbis" disclosure of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene" in Imler '143.**

18. Imler '143 describes

> ...the subject of the present invention ... [as] an adenoviral vector which is defective for replication, ..., [and] is derived from the genome of an adenovirus comprising, from 5' to 3', a 5' ITR [inverted terminal repeat], an encapsidation region, an E1A region, an E1B region, and **E2** region, an E3 region, an E4 region and a 3' ITR, by deletion of:
>
> (i) all or part of the E1A region and the whole of the portion of the E1B region coding for the early proteins; or
>
> (ii) all or part of the E1A region and all or part of at least one region selected from **E2** and E4 regions; or
>
> (iii) all or part of the E1A region and a portion of the encapsidation region (Ex 2002, p. 6, ll. 12-26, emphasis added).

* * * * * *

> Moreover, an adenoviral vector according to the invention is derived ... by deletion of all or part:
> - of the E3 region and/or
> - of the **E2** region and/or
> - of the E4 region (id., p. 7, l. 37 - p. 8, l. 4, emphasis added).
>
> * * * * * *
>
> ... a second variant, ... is derived ... by continuous or discontinuous deletion of all or part of the E1A region and all or part of at least the **E2** and/or E4 region (id., p. 9, ll. 2-7, emphasis added).

19. Imler '143 provides that:

> ..."deletion" or "lacking" refers to the elimination of at least one nucleotide in the target region, and the deletion can naturally be continuous or discontinuous. All or part is taken to mean either the whole or only a portion of the region in question. Deletions are preferred which prevent the production of at least one expression product encoded by the said region. Hence they may lie in a coding region or in a regulatory region such as the promoter region, and may affect at least one nucleotide so as to destroy the reading frame of a gene or render a promoter region non-functional. The deletions in question may also comprise partial deletions of one or more genes of the said region or of the whole of the region. [Ex 2002, p. 6, l. 27 - p. 7, l. 2.]

20. Imler '143 contains five examples drawn to deleted adenoviruses and three examples drawn to cell lines which complement for deleted adenoviral gene functions. Examples 1-5 are drawn to adenoviruses with deletion of (1) a portion of the encapsidation region, (2) the E1A region and the whole of the sequences coding for early proteins of the E1B region, (3) part of the E1 and E3 regions, (4) the E1 and E4 regions, and (5) all but the 5' and 3' ITR regions and the encapsidation region, respectively (Ex 2002, pp. 25-36). Examples 6-8 are drawn to cell lines capable of complementing (6) the E1 function, (7) all functions essential to the replication of an adenovirus, and (8) the E1 and E4 functions (id., pp. 36-49). There is no example of an E2A deleted recombinant adenovirus/adenoviral vector.

21. While several of the fifty-five originally filed claims in Imler '143 (i.e., original claims 1, 4, 6 and 33-35) recite deletion of all or part of "E2", none recite deletion of all or part of "E2A."

22. In the preliminary amendment of February 6, 1999, Imler added new claims 56-60 which contained explicit reference to the E2A gene region, i.e., claims 56-59 recited "wherein the function of an E2A gene is completely deleted by removing a part or all of said E2A gene" and claim 60 recited "an adenovirus genome having a foreign gene inserted between the termination codons of an E2A gene and an L3 gene" (Ex 2010, pp. 5-6).

23. Exhibit 2010 (p. 6) indicated that

> [s]upport for these new claims can be found throughout the subject application. For example, page 7, line 37, through page 8, line 8, of the specification discloses new replication defective adenoviral vectors whereby all or part of the E2 region is deleted. The specification, on at least page 2, line 38, through page 3, line 4, discloses that the products of the E2 region comprise two transcription units, E2A and E2B.

24. Neither of these two "supporting" cites identify E2A as the region intended for deletion. The former cite has been quoted above (fact 18). The latter cite describes region E2 as having two transcription units, E2A and E2B, which govern synthesis of a 72kDa DNA binding protein and a DNA polymerase which are involved in the replication of viral DNA. Thus, while the entire E2 region has been identified for total or partial deletion and at least two of the proteins encoded by the E2 region have been identified, neither the regions nor the nucleotides (i.e., coding and regulatory sequences) encoding them have been individually identified for deletion.

25. In the amendment filed October 27, 2000, Imler added new claim 61 which explicitly recited "removing a part or all of said E2A gene" (Ex 2017, p. 4).

26. Exhibit 2017 (p. 7) indicated that claim 61 was essentially previously added claim 58 written in independent form.

27. In the amendment filed May 10, 2001, Imler added new claims 62-65 which recited "removing all or part of said E2A gene" (Ex 2015, pp. 1-2).

28. Exhibit 2015 (p. 3) indicated that "[s]upport for the [new] claims can be found throughout the originally filed application including, for example, original claim 1."

29. Original claim 1 recites the "E2" gene region, not the "E2A" gene region.

Thus, there is no original ipsissimis verbis disclosure of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene."

However, ipsissimis verbis disclosure is not necessary to satisfy the written description requirement of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question. In re Edwards, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978).

**B. The specification of Imler '143 does not reasonably convey to one of ordinary skill in the art that Imler was in possession of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene."**

30. A person of ordinary skill in the field of recombinant adenoviral research at the time the Imler applications were filed was typically an M.D. or Ph.D. with training in

virology or related areas and at least two years of post-graduate experience in developing recombinant adenoviruses and vectors (see Paper 102, p. 2, where Wang admits Imler fact 6 as set forth in Paper 64, p. 4).

31. According to her curriculum vitae, Monika Lusky-Helm received a Ph.D. in molecular biology and genetics from the University of Freiberg in 1980 and was involved in research on the genetics and molecular mechanisms of bovine papilloma virus from 1980 through 1994. Dr. Lusky-Helm worked with adenoviruses and vectors at the adenovirology laboratory of TRANSGENE S.A. (Imler's assignee) from 1995 to the present. [Ex 1031, pp. 1-2.]

32. Dr. Lusky-Helm testified that she used adenoviral vectors, including E1 deletion vectors, in the 1980s and beginning 1990s as a tool to express other viral genes (Ex 2025, p. 13, l. 9 - p. 14, l. 5).

33. Thus, Dr. Lusky-Helm is a person of ordinary skill in the field of recombinant adenoviral research.

34. Dr. Lusky-Helm testified on behalf of Imler that

> It would have been apparent to a person of ordinary skill in the art, from the disclosure of the 1994 International Application Translation, the Imler '452 Application, and the Imler '143 Application, that the inventors in describing the deletion of all or part of the E2 region so as to create a replication defective recombinant adenovirus considered deletion of the function of the E2A gene by deletion of all or part of the E2A gene as an aspect of their invention. In the International Application No. PCT/FR94/00624 [Imler PCT], E2 is described as containing only the two transcription units E2A and E2B, and specifically refers to the essential protein synthesized in the E2A region. Given these disclosures those skilled in the art would have recognized that the inventors were in possession of an adenovirus wherein the function of an E2A gene is completely deleted by removing a part or all of the gene. [Ex 1032, ¶ 25.]

35. When asked how she came to the conclusion that Imler's applications describe a selective deletion of adenoviral gene region E2A, Dr. Lusky-Helm testified that she thought the disclosures rendered such selection obvious. However, Dr. Lusky-Helm could not find the relied upon disclosure when queried at cross-examination:

> Q: Other than the words deletion of all or part of E2, what in the 1993 application [Ex 1006] describes specifically the deletion of E2a?
>
> A: To my -- I think from my review of the application, it is obvious through the combination of various paragraphs that the only thing -- well, not the only thing. That is obvious to delete E2a and not other regions in E2.
>
> Q: Okay. What are the paragraphs that you were pointing to?
>
> A: Well, for example, it's kind of a series of paragraphs that start out broad and then narrow the whole thing sort of down. For example, in the beginning -- in the French application -- I'm not sure whether I find all of these now, because I haven't marked them, and besides these are your copies. In the beginning, it says -- first page of the application, the invention relates -- excuse me.
>
> I would have to look. I may -- excuse me, please. I would need to look for a while.
>
> Q: Are the relevant portions cited in your declaration?
>
> A: Just give me a minute.
>
> Q: Sure. Take your time.
>
> A: Well, for example, page 11, 3 to 5 -- lines 3 to 5 -- I may not find all of the citations, but I'm trying to find some at least. Furthermore, lines -- page 11, line 3 to 5, furthermore, a defective genome virus according to the invention can additionally lack all or part of the E2 region.[5]
>
> The product of the E2 region which also comprise -- no. There was another reference where the -- I will have to go through the --
>
> Q: Well, that's okay. [Ex 2025, p. 106, l. 20 - p. 108, l. 3.]

---

[5] "Furthermore, a defective adenovirus according to the invention can additionally lack all or part of the E2 region" (Ex 1006, p. 11, ll. 3-5).

36. Dr. Lusky-Helm further testified that deleting an entire gene region, e.g., E2, and successfully complementing for that deletion would not be predictive of the results and experiences involved in deleting a portion of that region, e.g., E2A (Ex 2025, p. 7, l. 2 - p. 8, l. 17).

However, a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of the invention. Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966. Further in view of the testimony of Dr. Lusky-Helm, it is not clear that Imler '143 would have even rendered the invention obvious. Thus, the textual disclosure of Imler '143 would not have reasonably conveyed to one skilled in the art that Imler was in possession of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene."

**C. Imler '143 Figure 1 does not describe or reasonably convey to one of ordinary skill in the art that Imler was in possession of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene."**

Drawings are also part of the original disclosure.

37. Figure 1 of Imler '143, Imler '452 and Imler PCT (Exs 2002, 2008 and 1004, Figure 1/11) "is a diagrammatic representation of the genome of the human adenovirus type 5 (represented in arbitrary units from 0 to 100), including the location of the different genes" (Ex 2002, p. 23, ll. 14-17). (Figures 2 through 11 do not relate to or otherwise describe the E2A gene region).

38. Imler '143 Figure 1 is reproduced below.

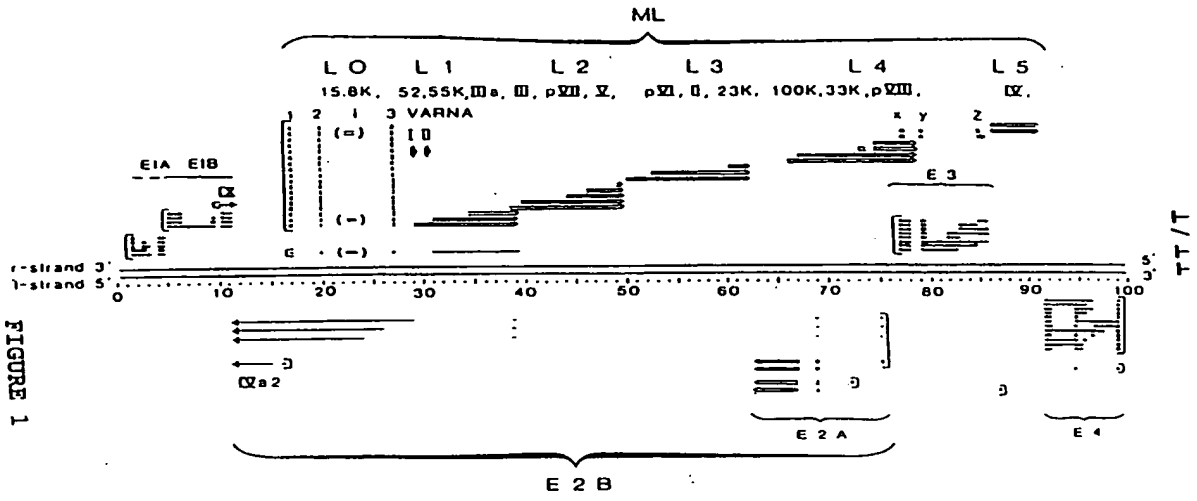


FIGURE 1

39. Imler Figure 1 indicates that region E2A is wholly contained within region E2B. In other words, Figure 1 indicates that deleting part or all of region E2A would result in deleting part of region E2B. Conversely, Figure 1 indicates that large parts of region E2B could be deleted without deleting any of region E2A.[6]

Thus, from Imler Figure 1, the testimony of Dr. Lusky-Helm and the limited reference to deletion of the **E2** region in Imler '143, it does not appear that one skilled in the art could reasonably conclude that Imler was in possession of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene."

40. Although Dr. Lusky-Helm testified that some deletions in the E2A region will not ablate the function of the E2B region, she also testified that the Imler application did not

---

[6] Wang preliminary motion 1 (Paper 34, p. 6, material fact 19) states "Moreover, the Board recognizes that vectors deleted of all E2 functions are patentably distinct from vectors wherein only E2A function is deleted. Paper 44, p. 9, ll. 5-10." However, Paper 44 is a joint stipulation to an extension of time filed by Imler on October 23, 2002. Therefore, this "fact" is incorrect on its face.

provide the necessary information to arrive at deletions which impact the functions of E2A but not E2B (see Ex 2025, pp. 95-102). For example,

> Q: ... Any deletion in the E2a region necessarily inserts a deletion in the E2b region. Right?
>
> A: Yes.
>
> Q: What deletion of these two regions will ablate the function of E2a but not E2b?
>
> A: A deletion of part or all of the E2a coding region; that is to say, within the sequences that code for the E2a DPT 72 kilodalton protein, within that region, you can delete all or part of that region and not affect any function of the E2b genes that is the DNA preliminaries [sic, polymerase?] and the pTG [sic] protein.
> [Ex 2025, p. 96, ll. 12-24.]
>
> * * * * * *
>
> Q: ... [C]an you delete a regulatory sequence required for E2a function without deleting E2b function?
>
> A: I would have to look at the splicing pattern.
>
> * * * * * *
>
> Q: This application does not provide the information necessary to arrive at a deletion of the regulatory sequence for E2a that does not also impact the regulatory sequence for E2b. Right?
>
> A: Yeah.
> [Ex 2025, p. 97, ll. 7-24.]

In its opposition, Imler argues that while Imler Figure 1 shows the E2A transcription unit wholly within the E2B transcription unit, the coding sequences of the E2A and E2B genes do not overlap (Paper 64, p. 13). This argument is based on the testimony of Dr. Lusky-Helm that "[t]he coding sequences of the E2A and E2B genes do not overlap, as shown by the Wang Submission of Glossary and Map [Paper 32] in the Table of Adenovirus Serotype 5 Coding Sequences" (Ex 1032, ¶ 16).

As noted by Wang in its reply (Paper 102, p. 7), Wang's map (Paper 32) is not part of the Imler disclosure. Later documents which add to the knowledge in the art cannot be used to supplement an insufficient disclosure. In re Glass, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974). Furthermore, Imler's own expert, Dr. Lusky-Helm, characterized Imler's map, i.e., Figure 1, as "schematic" and stated that "maps are something that develop ... that is in constant flow" as more knowledge is gained (Ex 2025, pp. 100-102[7]). Essentially, Imler is relying on those skilled in the art to figure out

---

[7] Dr. Lusky-Helm testified:

Q: ...do the coding sequences of E2a and E2b overlap?
A: To my belief, the coding sequences for adeno5 [sic] for E2a and E2b do not overlap.
Q: So in that respect, is figure 1 of Exhibit 1004 [certified English translation of Imler PCT] wrong?
A: Figure 1 of exhibit -- of this exhibit --
Q: Uh-huh.
A: -- is a figure that is taken from -- I can't recited the first publication but from a very old publication in the '70s or beginning of the '80s.
Q: And it's just inaccurate with respect to that overlap?
A: That I cannot judge, because it is very -- a schematic.
Q: Well, it definitely shows the coding sequences to overlap. Right?
A: No.
Q: There's no overlap between E2a and E2b here?
A: The coding sequences?
Q: Uh-huh.
A: No. I can't see an overlap of the coding sequences.
Q: Is there in fact outside of the shared leader sequences an overlap between the coding sequence of E2a and the coding sequence of E2b?
A: I don't see -- I don't -- to my belief, there is no overlap between the -- of the coding sequences of E2a and E2b.
Q: So this map is an accurate thing, is that correct, as of your knowledge of today?
A: This map is accurate as of the knowledge as its was at the time the map was made.
Q: But let's take it in stages. As of 1993 [when Imler FR '482 was filed], was this map accurate, of the knowledge and skill of those in the art?
A: Probably.
Q: Would that also be true of 1994 [when Imler PCT was filed]?
A: I guess so.
Q: How about 1996 [Imler '452 was filed in 1995]?
A: The answer to this question is very complicated, because maps are something that develop, and the principle of this map is accurate as of today [November 27, 2002]. As more and more knowledge is gained in resequencing certain regions, reanalyzing certain regions that hadn't been analyzed maybe 20 years ago when that map was first generated, the map has to be corrected. So a map is something that is in constant flow, if

what Imler didn't say, especially in regard to Imler Figure 1.

In view of the foregoing, we find nothing in the original disclosure of Imler '143, including its drawings, to indicate, explicitly or implicitly, that Imler had possession of a recombinant adenovirus/adenoviral vector "wherein the function of an E2A adenoviral gene is completely deleted by removing a part or all of said E2A gene." Thus, Imler claims 56-57, 59 and 61-65 are based on a specification which, as filed, does not satisfy the written description requirement of 35 U.S.C. § 112, first paragraph.

For the above reasons, Wang preliminary motion 3 is **granted**.

## IV. Wang preliminary motion 2

Wang moves pursuant to 37 CFR § 1.633(g) to attack the priority benefit accorded Imler of its earlier filed applications, i.e., Imler '452, Imler PCT and Imler FR '482 (Paper 33). Imler opposes (Paper 63); Wang replies (Paper 101). Wang contends that none of these three Imler priority applications constitute a constructive reduction to practice because none of these applications (i) provide an example of a deleted adenovirus where E2A, as opposed to E2 or E2B, has been deleted, or (ii) describe or address selective deletion of E2A (Paper 33, p. 10).

A party may be accorded benefit for the purpose of priority (i.e., a constructive

---

you wish.

Q: When was sufficient information accumulated to recognize that at least with respect to the E2 region, the map that is figure 1 needed to be corrected to be completely accurate?

MR. WALTERS: Objection. That mischaracterizes the figure.

THE WITNESS: I don't know. I cannot answer that question, because the map doesn't indicate where it is not correct, and even from today's knowledge, you couldn't know where the map is in -- where the map is, if at all, incorrect, because it's so schematic. You can't recognize from these arrows or something whether it's exactly map unit 60 or 60.05 or something.

[Ex 2025, p. 100, l. 12 - p. 102, l. 25.]

reduction to practice) of an earlier application if the earlier application contains a written description of the subject matter of the count and meets the enablement requirement. Hyatt v. Boone, 146 F.3d 1348, 1352, 47 USPQ2d 1128, 1130 (Fed. Cir. 1998). "It is insufficient as written description, for purposes of establishing priority of invention, to provide a specification that does not unambiguously describe all limitations of the count." Id., 146 F.3d at 1353, 47 USPQ2d at 1131.

Since the disclosures of Imler '143, Imler '452 and Imler PCT are identical, the above discussion of the Imler '143 disclosure also applies to the Imler '452 and Imler PCT disclosures.

41. As to Imler FR '482, the terms E2A and E2B are found in the following citations:

> In particular, the E1A transcription unit codes for a protein which trans-activates the transcription of the other viral genes, inducing transcription from the promoters of the E1B, E2A, E2B and E4 regions.
>
> The products of the E2 region, which also comprises two transcription units E2A and E2B, are directly involved in the replication of the viral DNA. This region governs, in particular, the synthesis of a 72 kDa protein which displays a strong affinity for single-stranded DNA, and of a DNA polymerase. [Ex 1006, p. 2, l. 36 - p. 3, l. 7.]
>
> * * * * * *
>
> ...Said gene [encoding for a selectable marker] maybe placed under the control of a constitutive promoter, especially the SV40 virus early promoter. However, a promoter which is inducible by the trans-activating protein encoded by the E1A region will be preferred, especially the E2A adenoviral promoter. [Id., p. 21, ll. 5-9.]

42. Example 3 in Imler FR '482 forms a "de minimus" adenoviral vector by assembling together (i) a 5' ITR region (ii) an encapsidation region, (iii) a exogenous nucleotide sequence, (iv) sequences encoding a yeast Gal4 protein under the control of a promoter, and (v) a 3' ITR region (Ex 1006, p.29).

43. Original claim 31 in Imler FR '482 recites a complementing cell line having a gene encoding a selectable marker, i.e., puromycin acetyltransferase, under the control of the E2A adenoviral promoter.

Imler FR '482 does not contain even a bald reference to an E2 deleted vector.

Both parties have presented substantially similar arguments, oppositions and replies regarding Imler '452 and Imler PCT as presented in regard to Imler '143 as discussed above in § III.

44. For example, in its opposition Imler argues

> Given the above disclosures [Imler '452 and Imler PCT which are identical to Imler '143], it would have been apparent to a person of ordinary skill in the art, from the disclosure of the Imler '452 Application and the Imler '624 PCT, that the inventors in describing the deletion of all or part of the E2 region so as to create a replication defective recombinant adenovirus considered deletion of the function of the E2A gene by deletion of all or part of the E2A gene as an aspect of their invention. Exhibit 1032, ¶ 25 [Dr. Lusky-Helm Declaration III]. Imler's Applications disclose that the invention relates to replication defective recombinant adenovirus wherein specific regions of the genome have been deleted. Exhibit 2008 [Imler '452], p. 5, ll. 35-39. Imler discloses that all or part of the E2 region can be deleted. Imler describes the two transcription units (sub-regions), E2A and E2B, which are parts of the E2 region. Further, Imler names an essential gene in each of the E2A and E2B transcription units. One of ordinary skill in the art would have understood that deletion of the function of the E2A gene by deletion of all or part of the E2A gene would result in a replication defective adenovirus. Exhibit 1032, ¶ 24. A deletion of part of the E2 region which produces a replication defective adenovirus must remove a function of E2A, E2B, or both subregions. Thus, the Imler '452 Application and the Imler '642 PCT Application, convey to a person of skill in the art that Imler was in possession of an adenovirus that falls within the scope of Count 1. Exhibit 1032, ¶ 5.
>
> Wang attempts to argue that, because the E2A transcription unit overlaps the E2B transcription unit, Imler could not be possession of an adenovirus enabling an E2A deletion. Wang asserts, in the paragraph bridging pages 12 and 13 of its motion, that "[t]he map provided by Imler (Fig. 1) places E2A wholly within E2B, with E2B extending well beyond E2A." This much is correct with respect to the E2A and E2B transcription

> units. However, in its motion, Wang fails to include the fact that the coding sequences of the E2A and E2B genes do not overlap. *See* Exhibit 1032, ¶ 16. Thus, a deletion in E2A that removes the entire function of the E2A gene does not require a deletion in E2B that affects a function of an E2B gene. Exhibit 1032, ¶ 17. Imler Claims 56 and 62, two of the three alternatives of Count 1, recite that "the function of an E2A gene is completely deleted by removing a part or all of said E2A gene." Thus, Wang's argument fails to show that Imler was not in possession of an adenovirus that falls within the scope of Count 1. [Paper 63, pp. 16-18.]

45. Imler further argues

> ... it would have been apparent to a person of ordinary skill in the art, from the disclosure of the Imler French Application, that the inventors, in describing the deletion of all or part of the E2 region so as to create a replication defective recombinant adenovirus, considered deletion of the function of the E2A gene by deletion of all or part of the E2A gene as an aspect of their invention. Exhibit 1032, ¶ 19. One of ordinary skill in the art would have understood that deletion of the function of the E2A gene by deletion of all or part of the E2A gene would result in a replication defective adenovirus. Exhibit 1032, ¶ 18. The essential 72 kDa protein product of the E2A gene region is one of two essential E2 genes specifically described by the Imler French Application. The other, DNA polymerase, is an E2B gene product. A deletion of all or part of E2 which produces a replication defective adenovirus must remove a function of either E2A, E2B, or both. Thus, the Imler French Application would convey to a person skilled in the art that Imler was in possession of an adenovirus that falls within the scope of Count 1. [Paper 63, p. 21.]

We incorporate our reasoning in § III above and add the following.

A deletion of all or part of E2 which produces a replication defective adenovirus must remove a replication "essential" function of either E2A, E2B, or both. On the one hand, removing an entire region, i.e., E2A, E2B or both (i.e., E2), and, thereby, removing its functions presents a very small number of possible deletions. On the other hand, there are an immense number of possible ways to delete at least one nucleotide from the E2 region without affecting the E2A region specifically.

In addition, Dr. Lusky-Helm testified that deleting an entire gene region, e.g., E2, and successfully complementing for that deletion would not be predictive of the results and experiences involved in deleting a portion of that region, e.g., E2A (Ex 2025, p. 7, l. 2 - p. 8, l. 17). Thus, deleting or removing all of E2 does not reasonably convey deletion "all or part of E2A." In particular, none of Imler '143, Imler '452, Imler PCT or Imler FR '482 explicitly describe or reasonably convey deletion of any part of E2A without a deletion of E2B.[8]

Imler's rebuttal arguments depend to a large extent on the opinion of Dr. Lusky-Helm that one skilled in the art would have known that the coding sequences of the E2A and E2B genes do not overlap and, therefore, a deletion in E2A that removes the entire function of the E2A gene does not require a deletion in E2B that affects a function of an E2B gene. However, Dr. Lusky-Helm's opinion is based on "the Wang Submission of Glossary and Map in the Table of Adenovirus Serotype 5 Coding Sequences" (Ex 1032, ¶ 16), not upon any Imler disclosure, e.g., identified drawings (Imler Figure 1) and/or specification cites in any of the Imler '143, Imler '452, Imler PCT or Imler FR '482 disclosures. See Glass, 492 F.2d at 1232, 181 USPQ at 34 (later references which add to the knowledge in the art cannot be used to supplement an insufficient disclosure).

To be sure, there is evidence of record that one skilled in the art knew that adenoviral early region E2 was comprised of two transcription units (E2A and E2B)

---

[8] Wang notes that Board has held that vectors deleted of all E2 functions are patentably distinct from vectors wherein only E2A is deleted and E2B is required in a copending interference 104,826 (Paper 33, pp. 5-6, "material fact" 17). The involved claims, facts and evidence in interference 104,826 are different from that presented in this interference. Therefore, we accord Wang's "argument" no weight.

encoding proteins known to be essential for viral replication as of the May 28, 1993 filing date of Imler FR '482. (See e.g., Berkner 1992[9] (Ex 2012, pp. 41-43)). Imler, however, fails to establish that one skilled in the art knew the location of the coding sequences within the E2A and E2B transcription units as of the respective filing dates of Imler '143, Imler '452, Imler PCT and Imler FR '482. To the contrary, Dr. Lusky-Helm testified that the gene "maps are something that develop ... that is in constant flow" as more knowledge is gained (Ex 2025, pp. 100-102).

In short, none of Imler's priority documents, Imler '452, Imler PCT or Imler FR '482, constitute a constructive reduction to practice of the Count because none provide an example of or reasonably convey possession of a replication deficient adenovirus/adenoviral vector wherein a function of the E2A gene is completely destroyed by selectively deleting all or part of the E2A gene.

For the above reasons, Wang preliminary motion 2 is **granted**.

## V. Imler preliminary motion 2

Imler moves pursuant to 37 CFR §§ 1.633(c)(2) and (i) to add proposed Imler claims 66 and 67 to Imler '143 in order to add proposed Count 2 directed to recombinant adenovirus/adenoviral vectors having deletions and/or mutations in both the E1 and E4 regions/genes[10] (Paper 50). Wang opposes (Paper 73). Imler replies (Paper 92).

---

[9] K.L. Berkner, "Expression of Heterologous Sequences in Adenoviral Vectors," Current Topics in Microbiology and Immunology, Vol. 158, pp. 39-66 (1992) (Ex 2012).

[10] An early region, e.g., E2A and E2B, contains one or more adenoviral genes and each gene encodes a functional protein or RNA molecule (Glossary, pp. 3 ("Early region") and 4 ("Gene")).

46. Proposed Imler claims 66 and 67 (Ex 1008) read as follows:

> 66. An adenovirus which is defective for replication, and which is derived from a natural adenovirus in that it lacks at least a part of the E1A, E1, or both regions, and at least a part of the E4 region, so that it is defective for the E1 and E4 functions and can be prepared by passage in a cell line providing the E1 and E4 functions *in trans*, and which comprises an exogenous nucleotide sequence.
>
> 67. A recombinant adenovirus comprising an adenovirus genome having a foreign gene and a promoter for expressing said foreign gene, wherein the function of an adenoviral E1 gene and an adenoviral E4 gene are completely deleted by removing a part or all of said E1 gene and said E4 gene.

47. Proposed Imler claims 66 and 67 would be identically incorporated into proposed Count 2 in the disjunctive (Ex 1007) and, therefore, would necessarily define the same patentable invention as proposed Count 2.

48. Finally, Imler has "shown the patentability" of proposed Imler claims 66 and 67 (Exs 1016 and 1017) in Imler '143.

Thus, Imler has satisfied the requirements of 37 CFR § 1.637(c)(2).

Wang argues that proposed (a) Imler claims 66 and 67 are unpatentable over prior art, (b) Imler claim 66 is not enabled for its full scope and (c) Imler claim 67 is neither enabled nor described (Paper 73, p. 7, ¶ 4).

**A. Wang's unpatentability argument fails because the primary prior art reference relied upon by Wang is not in evidence.**

49. Wang argues that proposed Imler claim 66 is anticipated by Exhibit 2021 (Bridge 1989[11]) or obvious over a combination of Exhibit 2021 with Exhibit 2011 (Berkner

---

[11] Bridge et al., "Redundant Control of Adenovirus Late Gene Expression of Early Region 4," Journal of Virology, Vol. 63, No. 2, pp. 631-638 (February 1989) (Ex 2021).

1988[12]) or 2012 (Berkner 1992[13]) (Paper 73, p. 5, ¶ 1). According to Wang, "Exhibit 2021, Figure 1, describes a mutant DL 1016, that satisfies all the requirements of proposed Claim 66, other than the recitation of the introduction of an exogenous nucleotide sequence. Exhibit 2025, Lusky, p. 23, ll. 2-15." [Paper 73, p. 2, material fact 2.] "With respect to the incorporation of exogenous DNA, [Dr.] Lusky [-Helm] testified that that was well known in 1993. Exhibit 2025, p. 23, ll. 16-20. Indeed, the same is described in prior art as early as 1988, Exhibit 2011 and again in 1992 in more detail, Exhibit 2012." [Paper 73, p. 4, last ¶.] Wang further argues that to the extent claim 67 provides both a foreign gene and a promoter for expression of said foreign gene, Exhibits 2011 and 2012 describe the same (Paper 73, p. 5, ¶ 3). Thus, Wang concludes that proposed Imler claims 66 and 67 are unpatentable over the prior art (Paper 75, p. 5, ¶¶ 2-3).

50. However, Bridge 1989 does not describe replication deficient adenoviral mutant dl1016 (or dl1018) in its FIG. 1 (Ex 2021, p. 632) or any place else so far as we see.

51. Moreover, Imler called the problem to Wang's attention in its reply. To wit,

> Imler notes that Wang misidentifies Exhibit 2021 in its Opposition. The paper that was labeled Wang Exhibit 2021 during the Deposition of Dr. Lusky-Helm is Bridge & Ketner, *Virology*, 174:345-63 (1990). From the context of the Deposition and the Opposition it is apparent that Wang is referring to this article. [Paper 92, p. 2, n.1.]

---

[12] K.L. Berkner, "Development of Adenovirus Vectors for the Expression of Heterologous Genes," BioTechniques, Vol. 6, No. 7, pp. 616-624, 626, 628, 630 (1988) (Ex 2011).

[13] K.L. Berkner, "Expression of Heterologous Sequences in Adenoviral Vectors," Current Topics in Microbiology and Immunology, Vol. 158, pp. 39-66 (1992) (Ex 2012).

52. We did not find a copy of Bridge & Ketner, Virology, 174:345-63 (1990) ("Bridge 1990") in the Wang '680 file at the Board.

53. In addition, since Imler's reply cites to copies of Office actions and Amendments, rather than to Bridge 1990 per se, it is not apparent to us that Imler had a copy of Bridge 1990 either.

It is Wang's burden to see that each prior art reference it relies upon is in evidence before the Board, particularly after Imler brought the apparent problem of Bridge 1990 to Wang's attention in its reply. There is no record of Wang requesting a conference call or taking any other action to correct this problem. Therefore, Wang's argument that proposed Imler claims 66 and 67 are unpatentable over the prior art fails because the relied upon prior art is not in evidence.

### B. Proposed Imler claim 66 is enabled when read in light of the express definition of an "exogenous nucleotide sequence" in Imler '143.

54. Wang further argues that proposed Imler claim 66 is not enabled because "if the exogenous nucleotide sequence [of the adenovirus] included a string of random nucleotides that do not direct expression of anything, or otherwise direct a function", "[s]uch an adenovirus would have no utility at all" (Paper 73, ¶ bridging pp. 5-6).

55. Imler '413 expressly defines an "exogenous nucleotide sequence"

> to mean a nucleic acid which comprises coding sequences and regulatory sequences permitting the expression of said coding sequences, and in which the coding sequences are sequences which are not normally present in the genome of an adenovirus (Ex 2002, p. 11, ll. 30-35).

Thus, when read in light of the Imler specification, proposed Imler claim 66 cannot encompass "a string of random nucleotides that do not direct expression of

anything, or otherwise direct a function." Therefore, this argument fails.

### C. Proposed Imler claim 67 describes and enables deletion of E1 and E4 gene regions.

56. Wang still further argues that "the sole difference between Claim 67 and 66 is that Claim 67 specifically requires deletion of genes from the region, as opposed to deletion of the region itself", and the Imler application does not describe deletion of a gene, as opposed to deletion of a region, or how to do so (Paper 73, p. 7, ¶3).

57. Imler '143 reads:

> For the purposes of the present invention, the term "deletion" or "lacking" refers to the elimination of at least one nucleotide in the target region, and the deletion can naturally be continuous or discontinuous. All or part of is taken to mean either the whole or only a portion of the region in question. Deletions are preferred which prevent the production of at least one expression product encoded by said region. Hence they may lie in a coding region or a regulatory region such as the promoter region, and may affect at least one nucleotide so as to destroy the reading frame of a gene or render a promoter region non-functional. The deletions in question may also comprise partial deletions of one or more genes of the said region or of the whole of the region. [Ex 2002, p. 6, l. 27 - p. 7, l. 2, emphasis added.]

58. Imler '143 also cites Genebank database reference M73260 and identifies nucleotide sequence 1634 to 4047 as "the whole of the portion coding for the early protein of the E1B region" and nucleotide sequence 505 to 4034 as "[comprising] neither the promoter sequences of the E1A region nor the transcription termination signal of the E1B region" (Ex 2002, p. 10, ll. 26-29 and p. 19, ll. 16-24) (in Imler FR '482, Ex 1006, see p. 9, ll. 16-20 and p. 18, ll. 29-34).

59. Further, the prior art describes constructing a series of adenoviral gene mutations in order to assign different roles to particular E4 gene products, see e.g.,

Figure 1 of Bridges 1989 (Ex 2021) which diagrams the positions of various E4 open reading frames in terms of adenovirus type 2 sequence map units.

60. At oral hearing, Wang stated "In Imler, as opposed to Wang, there's an emphasis on maximal deletion of gene regions" (Transcript, Paper 112, p. 10, ll. 16-17).

Thus, in our opinion, Imler '143, Imler '452, Imler PCT and Imler FR '482 all describe deletion of E1 and E4 gene regions to one skilled in the art. Removal of one or more nucleotides that results in an adenovirus that does not produce a particular gene product is understood to be a deletion of that gene function. Construction of adenoviral deletion mutants which delete a gene function appears to be within the skill in the art in view of the state of the prior art, e.g., Genebank database reference M73260 and Bridge 1989 (Ex 2021). Consequently, this argument fails.

For the above reasons, Imler preliminary motion 2 is **granted**.

## VI. Imler preliminary motion 1

Imler moves pursuant to 37 CFR §§ 1.633(c)(1) and (i) to add proposed Count 2, which encompasses adenoviral vectors having deletions and/or mutations in both the E1 and E4 regions, to the interference and to designate Imler claims 66 and 67 and Wang claims 37-38, 46-47 and 56 as corresponding to proposed Count 2 (Paper 49). Wang opposes (Paper 72); Imler replies (Paper 91).

61. Proposed Count 2 reads:

The adenovirus which is defective for replication of proposed Imler Claim 66.
or
The recombinant adenovirus of proposed Imler Claim 67.
or
The recombinant adenovirus of Wang Claim 37.
or

The recombinant adenovirus of Wang Claim 38.
or
The recombinant adenoviral vector of Wang Claim 46 wherein the two gene regions are E1 and E4.
or
The recombinant adenoviral vector of Wang Claim 47.

Imler preliminary motion 1, when considered in light of the evidence relied upon in support of the motion, satisfies the requirements of 37 CFR § 1.637(c)(1) and provides a sufficient prima facie basis for adding proposed Count 2.

Wang opposes this motion "on the grounds that Claims 66 and 67 are not patentable to Imler, as obvious over the prior art, not described, and indefinite" (Paper 72, p. 1). Wang advances the same arguments advanced in Wang opposition 2 -- alleging that (i) Imler claims 66 and 67 are unpatentable over the prior art, i.e., Exs 2021, 2011 and/or 2012, (ii) Imler claim 66 is not enabled, and (iii) Imler claim 67 is not enabled or described (Paper 72, pp. 3-7) as asserted above in Wang opposition 2 (Paper 73).

As pointed out by Imler in its reply (Paper 91, p. 1, ¶ 3), Wang has provided no further explanation or support for its allegation that Imler claims 66 and 67 are indefinite. As to the remaining unpatentability arguments (i) - (iii), Imler advances the same replies asserted above in Imler reply 2 (Paper 91).

We incorporate our reasoning in § V. above and add that unsupported attorney argument of unpatentability based on indefiniteness cannot take the place of evidence and is, therefore, accorded no weight. Further, in our opinion, a count directed to recombinant adenoviruses/vectors having deletions and/or mutations in both the E1 and E4 regions is appropriate. However, it is not appropriate to add such a count in this

interference for at least the following reasons.

First, Imler would be in the position of junior party with respect to Count 1, but in the position of senior party with respect to proposed Count 2.

Second, all of Imler claims corresponding to Count 1, i.e., Imler claims 56-57. 59 and 61-65, are unpatentable to Imler whereas none of Wang's claims corresponding to Count 1, i.e., Wang claims 46 and 56, have been shown to be unpatentable to Wang.

Third, Imler does not intend to present priority evidence as to Count 1; rather it intends to rely solely on the May 28, 1993 filing date of Imler FR '482 to prove constructive reduction to practice of the invention of Count 1 (Paper 38). None of Imler FR '482, filed May 28, 1993, Imler PCT, filed May 27, 1994, nor Imler '452, filed January 26, 1995, constitute a constructive reduction to practice of the invention of Count 1 for reasons given above (§ IV. Wang preliminary motion 2). Wang '680 was filed November 3, 1994. Wang has an earlier date of constructive reduction to practice of the invention of Count 1 than Imler. Thus, Wang is entitled to prevail on the issue of priority as to the invention of Count 1.

Dismissing Imler preliminary motion 1, subject to the APJ taking further appropriate action, i.e., declaring a new interference between the parties wherein the sole count was substantially identical to proposed Count 2 in accordance with Imler preliminary motion 1, would provide a final decision as to this interference and avoid having Imler be both senior and junior party in the same interference. Moreover, since both parties have had the opportunity for motions, oppositions, replies and testimony as to Imler preliminary motions 1 through 5, there appears to be no reason, absent a

showing of good cause, why the proposed new interference should not proceed directly to its priority phase. The parties already have copies of the involved files and have had the opportunity to review and act upon them.

Therefore, for the reasons given above, Imler preliminary motion 1 is **dismissed, subject to the APJ taking further appropriate action**.

## VIII. Imler preliminary motions 3 through 5

Imler preliminary motions 3 through 5, each request benefit for the purpose of priority of the filing dates of each Imler '452, Imler PCT and Imler FR '482. Wang opposes all three motions with the same unpatentability arguments set forth in Wang oppositions 1 and 2, i.e., that (i) Imler claims 66 and 67 are unpatentable over the prior art (Exs 2021, 2011 and/or 2012), (ii) Imler claim 66 is not enabled and (iii) Imler claim 67 is neither enabled nor described. Imler replies with the same rebuttals set forth in Imler replies 1 and 2. Therefore, we consider these three motions together.

Pursuant to 37 CFR § 1.633(f), Imler preliminary motion 3 requests benefit for the purpose of priority of the January 26, 1995 filing date of Imler '452 with respect to proposed Count 2 (Paper 51). Wang opposes, contending that Imler preliminary motion 3 is moot because proposed Imler claims 66 and 67 are not patentable to Imler (Paper 74). Imler replies (Paper 93).

Pursuant to 37 CFR § 1.633(f), Imler preliminary motion 4 requests benefit for the purpose of priority of the May 27, 1994 filing date of Imler PCT with respect to proposed Count 2 (Paper 52). Wang opposes, contending that Imler preliminary motion 4 is moot because proposed Imler claims 66 and 67 are not patentable to Imler (Paper

75). Imler replies (Paper 94).

Pursuant to 37 CFR § 1.633(f), Imler preliminary motion 5 requests benefit for the purpose of priority of the May 28, 1993 filing date of Imler FR '482 with respect to proposed Count 2 (Paper 53). Wang opposes, contending that Imler preliminary motion 5 is moot because proposed Imler claims 66 and 67 are not patentable to Imler (Paper 76). Imler replies (Paper 95).

Each of Imler preliminary motions 3 through 5, when considered in light of the evidence relied upon in support of the motion, satisfies the requirements of 37 CFR § 1.637(f) and provides a sufficient prima facie basis for granting Imler benefit for the purpose of priority of (3) the January 26, 1995 filing date of Imler '452, (4) the May 27, 1994 filing date of Imler PCT and (5) the May 28, 1993 filing date of Imler FR '482, respectively, as to proposed Count 2.

Wang opposes Imler preliminary motions 3 through 5 on the same grounds that it opposed Imler preliminary motions 1 and 2, i.e., that (i) Imler claims 66 and 67 are allegedly unpatentable over the prior art, i.e., Exs 2021, 2011 and/or 2012, (Papers 74-76 pp. 3-5), (ii) Imler claim 66 is allegedly not enabled (Papers 74-76, p. 5), and (iii) Imler claim 67 is allegedly not enabled or described (Papers 74-76, pp. 5-7).

Imler advances the same rebuttals that it presented in Imler replies 1 and 2 (Papers 93-95).

We incorporate our same reasoning set forth in §§ V. and VI. above in deciding that Wang did not satisfy its burden of persuasion that Imler claims 66 and 67 are unpatentable as argued by Wang. Therefore, for the reasons given above, Imler

preliminary motions 3 through 5 are **dismissed, subject to the APJ taking further appropriate action**.

## IX. Imler preliminary motion 7

Imler moves pursuant to 37 CFR §§ 1.633(c)(2) and (i) to add proposed new Imler claims 68 and 69, which recite that part of the E2 gene region (as opposed to deleting all or part of E2A), if Wang preliminary motion 2 or 3 is granted, in order to substitute proposed Count 3 for present Count 1 (Paper 55). Wang opposes (Paper 78); Imler replies (Paper 97).

62. Proposed new Imler claims 68 and 69 read as follows (Ex 1023):

> 68. An adenovirus which is defective for replication, and which is derived from a natural adenovirus in that it lacks at least part of the E1A, E1B, or both regions, and a part of the E2 region, which can be prepared by passage in a cell line providing the defective functions *in trans*, and which comprises an exogenous nucleotide sequence.
>
> 69. A recombinant adenovirus comprising an adenovirus genome having a foreign gene and a promoter for expressing said foreign gene, wherein the function of an adenoviral E1 gene is completely deleted by removing a part of said E1 gene and the function of an adenoviral E2 gene is completely deleted by removing a part of said E2 gene.

63. Proposed Imler claims 68 and 69 would be identically incorporated into proposed Count 3 in the disjunctive (Ex 1022) and, therefore, would necessarily define the same patentable invention as proposed Count 3.

64. Finally, Imler has "shown the patentability" of proposed Imler claims 68 and 69 (Exs 1028 and 1029) in Imler '143.

Thus, Imler has satisfied the requirements of 37 CFR § 1.637(c)(2).

Wang argues that (a) proposed Imler claims 68 and 69 do not interfere with

Wang's claims and (b) are not enabled throughout their scope, (c) Imler preliminary motion 6 is premature and (d) Dr. Lusky-Helm's Declaration (Ex 1024) is entitled to little weight.

Since a claim must be patentable before the question of whether it interferes with another's claim is addressed, we begin with Wang's patentability argument that proposed Imler claims 68 and 69 are not enabled throughout their scope.

"To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting from In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors are neither mandatory nor cumulative. Enzo Biochem Inc. v. Calgene, Inc., 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999).

**A. It would require undue experimentation to enabled proposed Imler claims 68 and 69 throughout their scope based on the Wands factors.**

**1. Claim breadth**

65. According to Imler '143 (Ex 2002, p. 2, ll. 22-27),

> [t]hree regions, E1, E2, and E4, respectively, are essential to the viral replication. Thus, if an adenovirus is defective for one of these functions, that is to say if it cannot produce at least one protein encoded by one of these regions, this protein will have to be supplied to it *in trans*.

Proposed Imler claim 68 encompasses any replication-defective adenovirus lacking at least a part of the (i) E1A and/or E1B and (ii) E2 regions. Deletion of at least a part of the E1A and/or E1B regions alone may be sufficient to remove a replication essential function complemented for by the complementing cell line recited in claim 68. Moreover, deletions which prevent the production of at least one expression product encoded by a particular adenoviral early region are simply preferred and not required (Ex 2002, p. 6, l. 27 - p. 7, l. 2). Thus, the replication deficiency of the adenovirus of claim 68 may have nothing, something or everything to do with its lack of a portion of the E2 region.

Proposed Imler claim 69 requires "the function of an adenoviral E1 gene ... and the function of an adenoviral E2 gene" to be removed by removing a part of the E1 gene (i.e., a part of the E1 region) and a part of the E2 gene (i.e., a part of the E2 region).

At the outset, proposed Imler claim 69 appears indefinite because both the E1 and E2 genes encode multiple expression products and recitation of "the function" lacks antecedent basis. Further, it appears that "the function" may or may not be a function

essential to viral replication because claim 69, unlike claim 68, does not require use of a complementing cell line for viral preparation and deletions are not required to prevent the expression of protein products encoded by an early region gene.

In any event, there are an enormous number of possible nucleotide deletions that may be made within the E1 and E2 regions which ostensibly provide recombinant adenoviruses within the scope of Imler claims 68 and 69. The linchpin question is whether one skilled in the art would know how to choose the operative embodiments embraced by these claims. See Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576-77, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971) (noting that although claims may read on some inoperative embodiments, this does not necessarily invalidate the claim if the necessary information to limit the claims to operative embodiments is known to a person of ordinary skill in the art).

**2./3. Amount of direction or guidance presented/Presence or absence of working examples**

The ability to choose operative embodiments focuses on at least two considerations -- (1) the ability to provide essential gene functions in trans in a complementing cell line in order to be able to propagate the claimed deletion adenoviruses and (2) knowledge of the adenoviral genome, including (a) where coding and regulatory sequences are within a given adenoviral region and (b) how a deletion within one region will affect, e.g., ablate, the function of another region, e.g., on the opposite DNA strand, in order to selectively delete the parts of regions whose function could be complemented in a cell line and avoid deleting portions of the E2 region that

might affect the function of other gene regions (e.g., see Imler '143 Figure 1 where late gene regions overlap the E2 region on the opposite DNA strand).

Wang argues that the skilled artisan cannot complement for a deletion of E2B. Wang further argues that according to Imler '143, a deletion in E2A cannot be effected without deletion of at least a portion of E2B. [Paper 78, p. 5, ¶¶ 2-3.]

Imler replies that "[by] its own terms, Claim 68 is restricted to adenoviruses lacking functions that can be complemented in a cell line" (Paper 97, p. 6, ¶ 2). However, just knowing what is desired is quite different from enabling its attainment. Imler further replies that "Claim 69 clearly refers to a deletion of part of a gene thereby excluding the removal of the entire E2 region or the entire E2B subregion" (id., p. 7, ¶ 2). This reply misses the mark. Logic dictates that removal of the entire E2 region or the entire E2B subregion would delete every essential function encoded by that (sub)region. The relevant question is whether or not Imler '143 provides sufficient blazemarks, e.g., location of coding and regulatory sequences, identifying which nucleotides within the entire E2 region or the entire E2B subregion are necessary to provide the essential gene functions of E2 or E2B (or E2A).

First, Imler points us to the "Wang Submission of Glossary and Map" (Paper 32) to show that the coding sequences of the E2A and E2B genes do not overlap. However, as noted above, the Wang map is not part of the Imler disclosure and cannot be used to supplement an insufficient disclosure. Glass, 492 F.2d at 1232, 181 USPQ at 34. Rather, Imler '143 Figure 1 (see fact 37) indicates that gene region E2A is wholly contained within gene region E2B and suggests that substantially all of the E2B gene

region is directly opposite late gene regions or promoter on the other DNA strand. Thus, the effect deleting any given part(s) of the E2 gene region might have on viral replication and complementation requirements appears to be highly unpredictable based on the scant Imler disclosure. Further, as stated above, according to Imler's own expert, Dr. Lusky-Helm, such maps are in a constant state of flow as regions are resequenced and reanalyzed (Ex 2025, pp. 100-102).

Second, there are no working examples of a dually-deleted, in whole or in part, E1 (E1A and/or E1B) and E2 adenovirus or complementing cells therefor in Imler '143.

Thus, Imler '143 provides little guidance or direction and no working examples of complementing for a deletion of an essential E2 function or for selecting operative deletions of part of the E1 and E2 regions/genes within the scope of claims 68 and 69.

**4./5. Relative skill of those in the art/State of the prior art**

Notwithstanding a relatively high level of skill in the art (as discussed above), the testimony of Dr. Lusky-Helm suggests that while the basic scheme of the adenovirus is known, the positions, sequences and interactions (i.e., splicing) of individual coding, regulatory and promoter sequences within the adenovirus genome is in a state of flux, constantly being updated as new knowledge is obtained, genes are resequenced and regions revisited.

**6./7./8. Predictability or unpredictability of the art/Nature of the invention/Quantity of experimentation necessary**

The double-stranded nature of the adenoviral genome means that one or more nucleotide deletions, continuous or discontinuous, in one part of one DNA strand may very well also affect the function of corresponding nucleotides on the other strand of

DNA. Moreover, even if expression of a particular gene product is not suppressed, the timing of its expression may be altered. Thus, complementation of deleted essential gene functions is highly complex because the proteins, etc. necessary for viral replication must not only be produced in sufficient quality, but also in a highly structured time frame.

In short, given these complexities, the unpredictability of the effect of deletions in one adenoviral (sub)region vis-a-visa another adenoviral (sub)region, the complexity of complementation expression and timing, and the constantly changing state of the art as well as the other Wands factors discussed above, in our opinion it would require undue experimentation to enable proposed Imler claims 68 and 69 throughout their scope.

Since proposed Imler claims 68 and 69 fail to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and are, therefore, unpatentable, it is not necessary to consider Wang's remaining arguments in order to decide this motion. We exercise our discretion and do not reach whether (a) there is no interference-in-fact between proposed Imler claims 68 and 69 and Wang claims,[14] (c) Imler preliminary motion 6 is premature or (d) Dr. Lusky-Helm's Declaration (Ex 1024) is entitled to little weight.

Therefore, for the above reasons, Imler preliminary motion 7 is **denied**.

---

[14] We note that a deletion of at least part of E1 and E2A as recited in Wang claim 46 anticipates removing a part of E1 and E2, which includes both E2A and E2B, as recited in proposed Imler claims 68 and 69. We also note that while anticipation requires a showing that each limitation of a claim is found in a single reference, the disclosure of a small genus may anticipate the species of that genus even if the species are not themselves recited. In re Petering, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962). Thus, since any deletion in E2 by definition must be a deletion in E2A and/or E2B, removing a part of E1 and E2 as recited in proposed Imler claims 68 and 69 might very well anticipate deleting at least a part of E1 and E2A, as recited in Wang claim 46.

## X. Imler preliminary motion 6

Imler moves pursuant to 37 CFR §§ 1.633(c)(1) and (i) to substitute proposed Count 3 for present Count 1, if Wang preliminary motions 2 or 3 is granted (Paper 54). Wang opposes (Paper 77); Imler replies (Paper 96).

66. Proposed Count 3 reads:

> The adenovirus which is defective for replication of proposed Imler Claim 68.
> or
> The recombinant adenovirus of proposed Imler Claim 69.
> or
> The recombinant adenoviral vector of Wang Claim 46 wherein the two gene regions are E1 and E2A.

67. According to Imler, proposed Imler claims 68-69 and Wang claims 46 and 56 should be designated as corresponding to proposed Count 3 (Paper 54, pp. 18-19).

Imler suggests that, in the event that Imler is not entitled to claims that specifically recite an E2A deletion, an interference between the Wang claims which recite a deletion of E1 and E2A and proposed Imler claims 68 and 69 which recite deletion of E1 and all or part of E2 would be appropriate and would allow Imler to rely on its best proof of priority of invention (Paper 54, pp. 1-2).

Wang opposes on the grounds that (1) there is no interference-in-fact between Wang claim 46 and proposed Imler claims 68 and 69, (2) proposed Imler claims 68 and 69 are not enabled throughout their scope, (3) Imler preliminary motion 6 is premature and (4) the three Dr. Lusky-Helm Declarations are entitled to little weight.

In order for there to be an interference between two or more applications, "interfering subject matter claimed in the applications" must be "patentable to each applicant subject to a judgment" on priority (37 CFR § 1.603). In view of our holding in

§ IX above that proposed Imler claims 68 and 69 are not patentable to Imler, Imler preliminary motion 6 is **denied**.

## XII. Imler preliminary motions 8 through 10.

Imler preliminary motions 8 through 10 each request benefit for the purpose of priority of the filing dates of each Imler '452, Imler PCT and Imler FR '482, respectively, with respect to proposed Count 3 (Papers 56-58). Thus, Imler preliminary motions 8 through 10 are contingent upon the grant of Imler preliminary motions 6 and 7.

In view of our decision denying Imler preliminary motions 6 and 7, Imler preliminary motions 8 through 10 are **dismissed** as moot.

## XIII. Miscellaneous

Imler filed "Imler Notice of Objections Pursuant to Oral Hearing" (Paper 113) objecting to (1) Wang's reliance on the purported testimony of Dr. Curiel, (2) Wang's reliance on the testimony of Dr. Ketner and (3) Wang's reliance on multiple Bridge and Ketner references at oral hearing. Wang replied in "Wang Response to Imler Notice of Objections" (Paper 114) that (1) it confused the testimony of Dr. Curiel with that of Dr. Lusky-Helm, (2) no testimony by Dr. Ketner has been presented to the Board in the context of this interference, (3)(i) arguments based on Exhibit 2024 (Bridge and Ketner 1989) were offered in rebuttal regarding the state of the art and (3)(ii) Imler had the opportunity to offer argument or observation with respect to Exhibit 2024 during its cross-examination of Dr. Lusky-Helm.

Imler's objections are moot because we did not rely on (1) any testimony from Dr. Curiel, (2) any testimony from Dr. Ketner or (3) Exhibit 2024 in reaching our decision.

**XIV. Order**

All of Imler's claims involved in the interference, i.e., Imler claims 56-57, 59 and 61-65, are unpatentable to Imler and none of Wang's claims involved in the interference, i.e., Wang claims 46 and 56, have been shown to be unpatentable to Wang. Normally, we would proceed to the priority phase of the interference where each party submits evidence to prove dates of invention. However, Imler does not intend to present priority evidence; rather it intends to rely solely the May 28, 1993 filing date of Imler FR '482 to prove constructive reduction to practice of the invention of Count 1 (Paper 38). However, none of Imler FR '482, filed May 28, 1993, Imler PCT, filed May 27, 1994 nor Imler '452 filed January 26, 1995, constitute a constructive reduction to practice of the invention of Count 1 for reasons given above. Wang '680 was filed November 3, 1994. Wang has an earlier date of constructive reduction to practice of the invention of Count 1 than Imler. Thus, Wang is also entitled to prevail on the issue of priority; hence, it is appropriate to enter a final decision.

We note that normally the APJ would issue an order to show cause why judgment should not be entered pursuant to 37 CFR § 1.640(d). However, in this particular case, especially since no further testimony is warranted, any response from Imler should be in the form of a request for reconsideration. Therefore, we are extending the time limit during which Imler may file a request for reconsideration from

the normal fourteen (14) days after the date of the decision to within twenty (20) days in keeping with the time limit for response to an order to show cause.

Therefore, upon consideration of the record, and for the reasons given, it is:

**ORDERED** that Wang preliminary motion 3 is **granted**.

**FURTHER ORDERED** that Imler claims 56-57, 59 and 61-65 are unpatentable under 35 U.S.C. § 112, first paragraph (lack of adequate written description).

**FURTHER ORDERED** that Wang preliminary motion 2 is **granted**.

**FURTHER ORDERED** that Imler '143 is not entitled to benefit for the purpose of priority of the filing dates of any of the Imler '452, Imler PCT or Imler FR '482 applications.

**FURTHER ORDERED** that Imler preliminary motion 2 is **granted**.

**FURTHER ORDERED** that Imler preliminary motions 1 and 3 through 5 are **dismissed, subject to the APJ taking further appropriate action**.

**FURTHER ORDERED** that Imler preliminary motions 6 and 7 are **denied**.

**FURTHER ORDERED** that Imler preliminary motions 8 through 10 are **dismissed**.

**FURTHER ORDERED** that judgment on priority as to Count 1 (Paper 1, p. 5) is awarded against senior party JEAN-LUC IMLER, MAJID MEHTALI and ANDREA PAVIRANI.

**FURTHER ORDERED** that senior party JEAN-LUC IMLER, MAJID MEHTALI and ANDREA PAVIRANI is not entitled to a patent containing claims 56-57, 59 and 61-65 (corresponding to Count 1). 35 U.S.C. § 112, first paragraph.

**FURTHER ORDERED** that Imler may file a request for reconsideration within twenty (20) days after the date of this order.

**FURTHER ORDERED** that if there is a settlement agreement and it has not already been filed, attention is directed to 35 U.S.C. § 135(c) and 37 CFR § 1.661.

**FURTHER ORDERED** that a copy of this decision be given appropriate paper numbers and entered into the file records of Wang application 08/333,680 and Imler application 09/218,143.

RICHARD TORCZON
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

BOARD OF PATENT APPEALS AND INTERFERENCES

cc (via overnight delivery):

Wang
(real party in interest
CELL GENESYS, INC.):

Steven B. Kelber, Esq.
PIPER MARBURY RUDNICK & WOLFE LLP
1200 Nineteenth Street, N.W.
Washington, DC 20036-2430
Tel: 202-861-3900
Fax: 202-223-2085
E-mail: steven.kelber@piperrudnick.com

Linda R. Judge, Esq.
CELL GENESYS, INC.
342 Lakeside Drive
Foster City, CA 94404
Tel: 650-425-4650
Fax: 650-349-7392
E-mail: linda.judge@cellgenesys.com

Imler
(real party in interest
TRANSGENE S.A.):

R.Danny Huntington, Esq.
Todd R. Walters, Esq.
Susan M. Dadio, Esq.
Norm H. Stepno, Esq.
Teresa Stanek Rea, Esq.
BURNS, DOANE, SWECKER & MATHIS, LLP
1737 King Street, Suite 500
Alexandria, VA 22313-2756
Tel: 703-836-6620
Fax: 703-836-2021
E-mail: dannyh@burnsdoane.com
toddw@burnsdoane.com
susand@burnsdoane.com
norms@burnsdoane.com
teresar@burnsdoane.com